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Policy: Can Access to Direct-to-consumer Pharmaceutical Advertising Classified as *Help-seeking* Improve Health on a Global Scale?

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1. Introduction

From a global perspective, pharmaceutical industry communications directly to consumers are generally uncommon. "The United States and New Zealand are the only two countries in the world where [all types of] direct-to-consumer (DTC) advertising of prescription drugs [are] legal."[1] The United States' Food and Drug Administration (FDA) has segmented DTC communication into product claims, product reminders, and help-seeking categories. FDA help-seeking communication is defined as non-branded disease state education, or health education without mention of a drug, therapy, or device. The elements of the Mexican framework focusing on "support [of] the patient, including, among others, these services:

[1] Lee, B. (2017, June 16). How Is Consumer Drug Advertising Regulated in the United States? https://goodrx.com. https://www.goodrx.com/blog/prescription-drug-advertising-regulation-united-states/

[reminders] of medical appointments, laboratory analysis, and [coaching] for a heathy life"[2] could serve as further definition. In the United States, the history of pharmaceutical advertising precedes the founding of the nation itself. "In the 1700s and 1800s drug compounds (also called "patent medicines") were advertised in newspapers in ways that were often exaggerated or deceptive."[3] A long tradition, "by the early 1900s, patent medication ads accounted for nearly half of the total ad revenue for newspapers."[4] "Over the next several decades, Congress recognized the distinction between over-the-counter medications and prescription drugs and, via the 1962 Kefauver-Harris Drug Amendments [8], authorized the FDA to regulate prescription drug marketing, while keeping over-the-counter drug advertising under the control of the Federal Trade Commission [1, 3, 8]. Through the 1962 Amendments, two requirements were set forth for prescription drug ads: (1) a drug advertisement must have a "summary" describing a drug's side effects, contraindications, warnings, and directions for use, and (2) the advertisement, as a whole, must provide a "fair balance" of information about a drug's effectiveness, safety, and risk [1, 3, 8]."[5] Bringing us to the current landscape, "in the late 1970s and early 1980s pharmaceutical companies began experimenting with advertising to customers through public relations techniques rather than paid ads."[6] In the case of New Zealand, the Medicines Act of 1981 legalized DTC. Attracting global attention, the World Health Organization has focused attention on American marketing practices.

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[2] Santillana Meneses, G. A. (2020, March). Pharmaceutical advertising 2020. Home | Global Practice Guides | Chambers and Partners. https://practiceguides.chambers.com/practice-guides/pharmaceutical-advertising-2020/mexico

[3] Jisu Huh, Denise E. DeLorme, Leonard N. Reid, and Soontae An, "Direct-to-Consumer Prescription Drug Advertising: History, Regulation, and Issues," minnesotamedicine.com, Mar. 2010

[4] Ibid.

[5] Weinmeyer, R. (2013, November). Direct-to-Consumer advertising of drugs. Journal of Ethics | American Medical Association. https://journalofethics.ama-assn.org/article/direct-consumer-advertising-drugs/2013-11

[6] Julie Donohue, "A History of Drug Advertising: The Evolving Roles of Consumers and Consumer Protection," Milbank Quarterly, ncbi.nlm.nih.gov, Dec. 2006

Around the globe, the European Union (EU) curtails pharmaceutical advertising, as do member countries. "Pharmaceutical regulatory systems in the EU are comprised of a decentralized body European Medicines Agency (EMA), Heads of Medicines Agencies (HMA), National Competent Authorities (NCAs) and European Directorate for the Quality of Medicines (EDQM). Eudralex is the collection of rules and regulations governing medicinal products in the EU."[7] In Asia, the Chinese Food and Drug Administration (CFDA) regulates the DTC market. In India, the Central Drugs Standard Control Organization (CDSCO) oversees DTC. A great number of countries around the world have their own specific pharmaceutical regulatory organization. In the absence of national pharmaceutical regulatory organizations, Ministries of Health perform the function. Like the complexities of the EU, every country around the world manages DTC in a unique manner. A global approach to DTC is so complicated, that national strategies are currently essential for global pharmaceutical marketers.

Hybrid DTC approaches around the world include countries such as Japan that permit certain types of DTC communication, but restrict branding and outright sales appeals. Disease state awareness and clinical trial recruitment are examples of types of DTC communications which are permitted in some parts of the world. South Africa stratifies medications, and restricts DTC around those available by prescription, compared to those off the shelf, or pharmacist dispensed medications. While Brazil disallows DTC advertising by industry, Brazilian regulation permits campaigns by their Ministry of Health to communicate the benefits of generic drugs.

A dramatic example of third world challenges, Amika Eze notes, "Nigeria [is faced with] many so called alternative medicine providers, … fleecing the unsuspecting drug consumers by

[7] Khanna, B. (2018, October). Pharmaceutical Medicine and Translational Clinical Research. https://www.sciencedirect.com/science/article/pii/B9780128021033000122.

aggressively marketing their drugs with spurious therapeutic claims,… [that many] of the drugs could pass as food supplements and vitamins."[8] "The providers claim omnibus, but untested potency for the drugs and … means of aggressive advertisement hoodwink the drug consumers to buy such drugs at very exorbitant prices. It is suggested that a complete ban of direct-to-consumer drug advertisement will help to rid the nation's drug market of fake, counterfeit and substandard drugs."[9]

2. Can Help-Seeking DTC Improve Global Health?

Much has been written about the controversy around product claim and product reminder (PCPR) DTC advertising of pharmaceutical products, the ethical nature of medical advertising, and whether it ought to be banned or protected. C. Lee Ventola has elucidated arguments in favor and against DTC. Accordingly, proponents of DTC as permitted in the United States argue education, improved compliance, lower cost through competition, decreased stigma, increased communication between patients and physicians, and benefits to patients who may otherwise not seek treatment justify DTC. Arguments against American DTC cite misinformation, questions around necessity, over-utilization, wasted valuable clinical time, and misallocation of healthcare spend. From a philosophical perspective, robust arguments can be made that educated health consumers have a greater ability to express autonomy. Through increased health literacy, people can make more informed decisions in their care, taking fuller advantage of what beneficence the healthcare system can provide. Health literacy can also reduce medical errors. With health disparities from nation to nation, a strong argument can be made that global help-seeking DTC

[8] EZE Amika G. (2016, January). International Journal of Business & Law Research 4(1):1-8. seahipaj.org. https://seahipaj.org/journals-ci/mar-2016/IJBLR/full/IJBLR-M-1-2016.pdf
[9] Ibid.

campaigns may have the ability to increase health literacy universally, satisfying justice principles philosophically.

Within the context of the American regulatory model, does FDA categorized help-seeking DTC have promise to improve health around the world? If so, what would be the pathway to realizing the benefit? Within the context of ethical frameworks, a review with commentary on the current DTC landscape, effectiveness, audiences, regulation, and legal frameworks, seeks to address the question.

3. Ethics of DTC

Healthcare is a Fundamental Human Right

Whether approached from secular or non-secular views, the arguments in favor of rights to healthcare outweigh the counterarguments. According to Peel, the right has conceptual origins in "documents [such] as the *Code of Hammurabi* (1780 BCE), Aristotle's *Nichomachean Ethics* (330 BCE), … [and] the Magna Carta (1215)."[10] The United Nation's Declaration on Human Rights (1948) states "everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care."[11] Pope Francis, speaking in 2016, noted to members of Doctors with Africa that "health is not a consumer good, but rather a universal right, and therefore access to health care services cannot be a privilege."[12] Counterarguments skirt morality, and cite legal technicalities such as

[10] Peel, M. (2005, April). Human rights and medical ethics. PubMed Central (PMC). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1079446/
[11] The United Nations. (2020, June 1). Universal Declaration of Human Rights. Welcome to the United Nations. https://www.un.org/en/universal-declaration-human-rights/
[12] Bergoglio, J. M. (2016, May 7). Health is a universal right, and access to healthcare services cannot be a privilege, says The Pope to the members of doctors with Africa (CUAMM). Bollettino. https://press.vatican.va/content/salastampa/en/bollettino/pubblico/2016/05/07/160507c.html

absence from the United States Constitution. Other counterarguments based on conscription, access, politics, or economics also lack morality.

"Health care, especially at the most basic level, is indeed denied in many parts of the world… Access to health care services, treatment and medicines remains a mirage. The poorest are unable to pay and are excluded from hospital services, even the most essential primary care."[13] From a moral perspective, provided health information is fair and balanced, pharmaceutical industry sponsored help-seeking DTC can work to achieve this fundamental human right. Whether viewed through industry or academic philosophic views, significant common ground should be exploited to affect positive change.

Consequentialism

"Consequentialism, as its name suggests, is simply the view that normative properties depend only on consequences. This historically important and still popular theory embodies the basic intuition that what is best or right is whatever makes the world best in the future, because we cannot change the past, so worrying about the past is no more useful than crying over spilled milk. This general approach can be applied at different levels to different normative properties of different kinds of things, but the most prominent example is probably consequentialism about the moral rightness of acts, which holds that whether an act is morally right depends only on the consequences of that act or of something related to that act, such as the motive behind the act or a general rule requiring acts of the same kind."[14]

[13] Bergoglio, J. M. (2016, May 7). Health is a universal right, and access to healthcare services cannot be a privilege, says The Pope to the members of doctors with Africa (CUAMM). Bollettino.
[14] Stanford Encyclopedia of Philosophy. (2003, May 20). Consequentialism (Stanford encyclopedia of philosophy). https://plato.stanford.edu/entries/consequentialism/

Through consequentialism, a judgement could be made that the means of creating help-seeking DTC, accepting sponsorship through pharmaceutical companies, is justified by the outcome of greater global health via health education. Conversely, a counterargument might suggest that the burden to industrialized countries, in the form of increased drug prices, is unfair and unwarranted.

Principlism

The Georgetown principles, or principlism, offers the most robust ethical framework to assess help-seeking DTC. Through principlism, we view the morality of help-seeking DTC through the principles of autonomy, beneficence, non-maleficence, and justice. More than a binary position, help-seeking DTC can achieve each of the principles. Autonomy addressed through the freedom to information, beneficence through the realization of putting help-seeking DTC to work for patients, minimizing maleficence through third party independence, and justice through increases in equity, all point to help-seeking DTC being a positive step in global health. Including a restorative justice principle, while no singular ethical crime has been committed by the pharmaceutical industry, global history has no doubt concentrated pharmaceutical development in wealthy industrialized countries. An obligation exists from a restorative justice principle to benefit all peoples, regardless of their nation, culture, or origins.

The Individual

Philosophical arguments regarding PCPR and help-seeking DTC are surprisingly less robust in volume than would be expected. While literature exists, most current work stems from popular media and business ethics organizations. According to Womak, "[a]rguments for and against direct-to-consumer drug advertising (DTCA) center on two issues: (1) the epistemic

effects on patients through access to information provided by the ads; and (2) the effects of such information on patients' abilities to make good choices in the healthcare marketplace. Advocates argue that DTCA provides useful information for patients as consumers, including information connecting symptoms to particular medical conditions, information about new drug therapies for those conditions."[15] Womak suggests the typical philosophical framework presumes a relationship in which more information equates to greater agency for patient. Citing empirical studies on medical decision making, Womak further asserts the relationship between information and patients' independence is "complex and nuanced" and that consideration for the conditions under which decisions are made is an aspect of the equation. As opposed to the American industry approach that DTC is driving conversation and exchange of information, Womack in effect suggests the patient has made up their mind in an autonomous fashion, without that very dialogue. As discussed in the context of audiences, Womak's assertion that "this requires examining both the cognitive limitations of patients with respect to drug information and investigating patients' preferences and needs in a variety of medical contexts"[16] is a fair concern.

Zadeh and colleagues evaluated 'At-risk' individuals' responses to direct-to-consumer advertising of prescription drugs from a nationally representative cross-sectional perspective. They concluded, "taken together, the findings suggest individuals, especially those who are 'at-risk' (ie, with poorer self-reported health status, older, less educated, lower income and ethnic minorities), may be more vulnerable to drug advertising and may make uninformed decisions accordingly. The outcomes raise significant concerns relating to the ethicality of drug advertising

[15] Womak, C. A. (2013, April 16). Ethical and epistemic issues in direct-to-consumer drug advertising: where is patient agency? PubMed. https://pubmed.ncbi.nlm.nih.gov/23526336/
[16] Ibid.

and suggest a need for stricter guidelines to ensure that drug advertisements provided by pharmaceutical companies are ethical."[17]

Ignoring individual autonomy, current laws and regulations around the world curtailing help-seeking DTC run the risk of paternalism. Applied to the four models of the physician-patient relationship, as described by Emanuel and Emanuel, "the paternalistic model is [only] justified during emergencies when the time taken to obtain informed consent might irreversibly harm the patient."[18] With help-seeking DTC, a direct relationship between pharmaceutical companies and patients is rife with conflicts of interest. Detractors argue conflicts of interest with pharmaceutical companies are too great to overcome to permit any type of relationship. Proponents would counter the bias of industry is too obvious for patients to ignore. Two-way communication between pharmaceutical companies and patients very likely represents one-way communication in reality because of imbalances in capacity and vulnerabilities. Any recommendation embracing help-seeking DTC must account for power inequities.

Ethics Applied to Industry

Concordant with their ethical mission statements, pharmaceutical companies have an obligation to provide education to consumers. The economic means of the pharmaceutical industry in a global context places material costs largely on wealthy developed nations. Yet even in developed countries, health education remains a low priority in curriculums. In many parts of the world, no access to health education is available. In the absence of state sponsored health education, regulated industry sponsored help-seeking DTC is a step forward.

[17] Zadeh, N. K. (2017, December 1). 'at-risk' individuals' responses to direct-to-consumer advertising of prescription drugs: A nationally representative cross-sectional study. BMJ Open. https://bmjopen.bmj.com/content/7/12/e017865
[18] Veatch RM. A Theory of Medical Ethics. New York, NY: Basic Books Inc Publishers; 1981.

In the United States, the Pharmaceutical Research and Manufacturers of America (PhRMA) trade association collectively represents the majority of large pharmaceutical companies. Conceived in 1958, PhRMA, formerly the Pharmaceutical Manufacturers Association, has been largely successful in maintaining the freedom of pharmaceutical companies to market medicines in the United States. PhRMA publishes an annual report on DTC which is based upon their guiding principles.

"These Principles are premised on the recognition that DTC advertising of prescription medicines can benefit the public health by increasing awareness about diseases, educating patients about treatment options, motivating patients to contact their physicians and engage in a dialogue about health concerns, increasing the likelihood that patients will receive appropriate care for conditions that are frequently under-diagnosed and undertreated, and encouraging compliance with prescription drug treatment regimens."[19] In adherence to FDA regulations, PhRMA principles state that DTC advertising ought to be consistent with product labeling, should be balanced, and maintain accuracy. With any DTC advertisement of a drug, PhRMA suggests it is only ethical to co-promote education about the disease which is being treated, and distinguish prescription from non-prescription products. "DTC television and print advertising should foster responsible communications between patients and health care professionals to help patients achieve better health and a more complete appreciation of both the health benefits and the known risks associated with the medicine being advertised. [20]

[19] PhRMA. (2017). Report of the PhRMA Member Signatory Companies to the PhRMA Guiding Principles on Direct-to-consumer Advertisements (DTC) about Prescription Medicines, Volume XIII. PhRMA Org | PhRMA. Retrieved January 24, 2021, from https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/V-Z/Vol-13-PhRMA-DTC-Guiding-Principles-Report-2017.pdf
[20] Ibid.

As stated in PhRMA's Guiding Principles on (DTC) about Prescription Medicines, pharmaceutical companies have an ethical responsibility to educate health care providers about DTC campaigns prior to their launch so as to provide appropriate background to professionals. In creating a balance, companies ought to consider professional education lead times relative to the complexity of a new drug being introduced through DTC. As was the case with the novel oral anticoagulants, DTC campaigns were withheld in the first year of each product's launch. Education should follow as new information becomes available about products, discontinuation of DTC is appropriate when new serious safety risks present, and all DTC should be submitted to FDA prior to release. PhRMA also maintains DTC is an opportunity to enhance adverse event capture and reporting with the inclusion of FDA's MedWatch information.

The Guiding Principles also state there should be respect for the severity of disease and targeting of DTC should be appropriate to the appropriate market segments. "In particular, DTC television and print advertisements containing content that may be inappropriate for children should be placed in programs or publications that are reasonably expected to draw an audience of approximately 90 percent adults (18 years or older)."[21] Aspiring to a philosophical justice principle, "companies should include information in all DTC advertising, where appropriate, about help for the uninsured and underinsured."[22] Manufacturers around the world echo many of the views held by PhRMA.

Globally, pharmaceutical manufactures have a legacy of organization for the betterment of patients. The Indian Drug Manufacturers association dates to 1961, and Japan's Japan Pharmaceutical Manufacturers Association (JPMA) has just celebrated 50 years. "The European

[21] Ibid.
[22] Ibid.

Federation of Pharmaceutical Industries and Associations (EFPIA) is a Brussels-based trade association founded in 1978 representing the research-based pharmaceutical industry operating in Europe."[23]

The JPMA perspective on demand creation is noteworthy. "To 'induce the use of' means to convince someone to use. Even if we can encourage the use of medicines, the reality is that we cannot create the demand. This is because consumers of prescription drugs are limited to patients who need treatment, and sales promotion cannot create patients. Inducing the use of medicinal drugs is permissible only when proper drug information is provided, because without it, the products cannot function as 'medicine'"[24]

There is far more philosophical common ground than might be expected with help-seeking DTC. Concerns expressed by Womak and Zadeh can be addressed by supporting agency and autonomy through unbiased health education. While industry may have more laissez-faire views, as expressed as principles around PCPR DTC, agreement can surely be reached around help-seeking DTC and the core principles of autonomy, delivering beneficence, reducing maleficence, and supporting global justice.

4. The Current Landscape: An Opportunity

DTC "advertising of drugs has been legal in the USA since 1985, but only really took off in 1997 when the FDA eased up on a rule obliging companies to offer a detailed list of side-

[23] European Federation of pharmaceutical industries and associations. (2006, October 18). Wikipedia, the free encyclopedia. Retrieved January 24, 2021, from https://en.wikipedia.org/wiki/European_Federation_of_Pharmaceutical_Industries_and_Associations

[24] Japanese Pharmaceutical Manufacturer's Association. (2019). Code of Practice. 日本製薬工業協会. https://www.jpma.or.jp/english/policies_guidelines/pdf/code_practice201910.pdf

effects in their infomercials (long format television commercials)."[25] Multichannel pharmaceutical marketing plans have evolved over the past twenty years. Ratios of advertising, direct marketing, sales promotion, publicity/public relations, and personal selling are less than static. As physical access to clinicians has decreased because of increased demands on physicians' time, and changes in the structure of healthcare delivery, so too has personal selling decreased. Virtual internet based approaches, and DTC are logically on the rise in the United States. "Indeed, there has been a remarkable increase in … DTC prescription drug marketing budgets over the years, skyrocketing from $1.3 billion in 1997 to over $6 billion in 2016 — a 361 percent increase."[26] Because of the global pandemic of 2020, the push towards DTC, virtual engagement, and digital strategies has further accelerated. The mix of therapeutic categories advertised via DTC is evolving. According to Dunn's 2019 report for Syneos, "The three therapeutic categories that decreased since 1997 were drugs for allergies, cholesterol and osteoporosis — all areas where blockbuster drugs lost patent protection or became over-the-counter medicines over those two decades, such as statins and antihistamines."[27] Interestingly, in part due to guaranteed reimbursement, DTC has increased in the HIV/AIDS and oncology markets. This despite often marginal benefits in the oncology market, and stigma surrounding HIV/AIDS. Case examples Opdivo + Yervoy costing $12,500.00 monthly, and Dovato $2648.00 monthly, illuminate the relationship between return on investment and the promotional mixes in the media. A basis for estimating the value of educational spend, "pharmaceutical and medical device company contributions accounted for 28% of [American physicians'] continuing

[25] Humphreys, G. (2009, August). Direct-to-consumer advertising under fire. WHO | World Health Organization. https://www.who.int/bulletin/volumes/87/8/09-040809/en/
[26] Shirola, W. (2020, February 3). U.S. should ban direct-to-consumer prescription drug advertisements. The Daily Northwestern. https://dailynorthwestern.com/2020/02/03/opinion/
[27] Dunn, A. (2019, January 7). Pharma DTC spending outpaces rest of medical marketing, JAMA study finds. BioPharma Dive. https://www.biopharmadive.com/news/pharma-dtc-spending-outpaces-rest-of-medical-marketing-jama-study-finds/545441/

medical education (CME) funding last year, according to the Accreditation Council for Continuing Medical Education 2017 annual report. Industry donors gave nearly $740 million to 1,794 accredited CME providers in 2017 — the fourth consecutive yearly increase."[28]

Regulations prohibiting product claims and product reminder DTC have drastically curtailed the same type of pharmaceutical speech on a global level. The current landscape of global DTC is conceptual, based upon marketplace forecasts and potential rather than historical or current spending. Global data on DTC spend could be segmented by North America, Europe, Asia Pacific, Latin America, and the Middle East & Africa. Clearly, further delineation of DTC approaches will vary from nation to nation. Because of prohibition, calculation of theoretical marketplace size around the world could best be modeled from the American and New Zealand experiences. The DTC market, if globalized according to the American model, would be on an incredible scale.

Pharmaceutical industry balance sheets are leaner than decades ago. According to csimarket.com, in terms of opportunity cost of capital, healthcare returns (7.6%) are greater than transportation (6.9%), and consumer discretionary sectors (4.1%).[29] However pressure on healthcare balance sheets is real compared to returns by technology (33.9%), services (20.8%), and basic materials (11.4%).[30] Given the ethical stance of healthcare, reallocation of sales and marketing expenses is still realistic. 10% of spend can be partially reallocated to shift DTC away from PCPR, towards help-seeking messages increasing net benefit. With pharmaceutical

[28] Pifer, R. (2018, July 26). *Pharma, medtech spending accounted for 28% of CME funds in 2017*. Healthcare Dive. https://www.healthcaredive.com/news/pharma-medtech-spending-accounted-for-28-of-cme-funds-in-2017/528598/

[29] CSI Market. (2021). Return on investment screening, rankings of best performing companies, sectors, industries. CSIMarket - Company, Sector, Industry and Market Analysis. https://csimarket.com/screening/index.php?s=roi

[30] Ibid.

business being a balance between the expense of research and development, operations, and returning profit, return on investment can be preserved through growth while achieving morally based mission goals through the provision of unbiased patient education.

5. Historical Effectiveness and Clinical Impact of PCPR DTC

Effectiveness is central to a discussion of DTC's impact on clinical decision making. Becker's systematic review of psychiatry-relevant studies sought to evaluate the effects of DTC on patient prescription requests and physician prescribing finding, "due to lack of replication across strong randomized controlled trials (RCTs), no conclusions merited high confidence. With moderate confidence, we concluded that DTCA requests: 1) are granted most of the time [1 RCT, 3 observational]; 2) prompt higher prescribing volume [1 RCT, 1 observational]; 3) promote greater adherence to minimally acceptable treatment guidelines for patients with depression [1 RCT], and 4) stimulate overprescribing among patients with an adjustment disorder [1 RCT]"[31] Becker concluded "more methodologically strong studies are needed to increase confidence in conclusions."[32]

For the Regulatory Affairs Professional Society, Mezher reported on a broader review conducted by "researchers at RTI International and the US Food and Drug Administration (FDA), [that] looked at 38 studies published between 1982 and 2017 [examining] outcomes reported by patients, prescribers or both regarding their experience with DTC advertising in the US and New Zealand."[33] Echoing Becker's conclusions, "When it comes to patients requesting

[31] Becker, S. (2016, October). Effects of direct-to-Consumer advertising on patient prescription requests and physician prescribing: A systematic review of psychiatry-relevant studies. PubMed Central (PMC). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5293137/
[32] Ibid.
[33] Mezher, M. (2019, April 18). DTC drug advertising: Study finds mixed impact on patients, prescribers. Regulatory Affairs Professionals Society | RAPS. https://www.raps.org/news-and-articles/news-articles/2019/4/dtc-drug-advertising-study-finds-mixed-impact-on

prescription drugs or changes to their prescriptions, the authors found varying results across the studies they looked at. While the previously mentioned 2004 FDA study found that less than one-third of patients sought a drug to treat their condition after seeing or hearing a DTC advertisement, another larger study found that more than half of respondents requested one or more medical interventions as a result of DTC advertising."[34]

From the physicians' perspective, as recently as 2002, *thepharmaletter* noted "the majority of US physicians questioned in a recent study said they believed that patients' awareness of direct-to-consumer advertising of prescription drugs has a beneficial effect on office visits."[35] By 2015, the American Medical Association (AMA), by majority vote, called "for a ban on all direct-to-consumer advertising for drugs and medical devices."[36] "The reason? AMA board chair-elect Patrice Harris said physicians are [now] concerned 'about the negative impact of commercially-driven promotions and the role that marketing costs play in fueling escalating drug prices,' in a news release."[37]

With the rise of patients' autonomy since the 1960s, "the shift has resulted in a quiet but dramatic transformation of the whole of our health care system. Gone is the time when doctors held complete power and prescription medicines were treated as a sacred and separate world."[38] Time constraints may hold another key. "In a 2017 survey of more than 1,000 physicians on the athenahealth network, six out of ten agreed with the statement, 'My visits with patients are often

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[34] Ibid.
[35] The Pharma Letter. (2002, February 25). US physicians back DTC ads: Study - Pharmaceutical industry news. Authoritative Pharma and Biotech News - The Pharma Letter. https://www.thepharmaletter.com/article/us-physicians-back-dtc-ads-study
[36] Bulik, B. S. (2015, November 17). Updated: Just say no to drugs (advertising): AMA votes to ban DTC ads. FiercePharma. https://www.fiercepharma.com/dtc-advertising/updated-just-say-no-to-drugs-advertising-ama-votes-to-ban-dtc-ads
[37] Ibid.
[38] Belkin, L. (n.d.). Prime Time Pushers. Mother Jones. https://www.motherjones.com/politics/2001/03/prime-time-pushers/

too short for me to answer their questions and treat them effectively.' Along similar lines, earlier research by athenahealth and others shows that primary care doctors are doing more work during each patient encounter, even as appointments have shrunk to 15 minutes or less."[39] Lack of consistent effectiveness data suggests that effectiveness measurement must accompany a global help-seeking DTC approach to ensure resources spent have tangible returns.

6. Audiences: Focus on Addressing Lay Vulnerabilities

It is a misnomer that DTC is solely intended for patients; the medical community are being targeted as well. Medical professionals and the lay public have vastly different capacities for understanding the medical literature and medical communication. We must take these differences in capacity into account on the issue of DTC. It is only logical to expect those in the medical profession to have the skills to evaluate medical advertising. At least in the United States, continuing medical education requirements serve to force physicians to remain current, however bias related to physicians' initial training in medical school and residency remain treatment anchors.

In the American lay population, "some of the greatest disparities in health literacy occur among racial and ethnic minority groups from different cultural backgrounds and those who do not speak English as a first language. Results from the US National Assessment of Adult Literacy demonstrated that Hispanic adults have the lowest average health literacy scores of all racial/ethnic groups, followed by black and then American Indian/Alaska Native adults."[40] Undermining health science literacy, according to the 2009 American National Center for

[39] DTC: Why do doctors fight it? (2019, March 11). World of DTC Marketing.com. https://worldofdtcmarketing.com/dtc-why-do-doctors-fight-it/

[40] Kutner M, Greenburg E, Jin Y, Paulsen C. The health literacy of America's adults: results from the 2003 national assessment of adult literacy. National Center for Education Statistics; 2006. Report No.: NCES 2006-483.

Educational Statistics, 11% of high school students studied statistics, and 16% of high school students studied calculus. Only 61.28 percent of Americans over the age of 25 have some college experience as reported by the US Census Bureau in 2018. With the United States ranked 8th in the world, according to the National Science Board, only 23% of American Undergraduates were enrolled in STEM in 2016.

From a global perspective, "only 6.7% of the world population has a Bachelor's degree."[41] On an annual basis, the United Nations publishes an education index as a part of the Human Development Index. "Since 2010, the Education Index has been measured by combining average adult years of schooling with expected years of schooling for children, each receiving 50% weighting. Before 2010, the Education Index was measured by the adult literacy rate (with two-thirds weighting) and the combined primary, secondary, and tertiary gross enrollment ratio (with one-third weighting)."[42] With only 19 of 188 countries mean years of schooling at 12 in the year of 2015, a dramatic gap exists on a global level compared to the United States.

Health literacy is not the only vulnerability that places the lay-person at a disadvantage in the world of DTC. According to Kipnis', "The Taxonomy of Vulnerability", lack of satisfactory therapies or options, situational urgency of medical needs, basic understanding and ability to assent/dissent, subordination to formal authority, deferential social pressures and influences, being a member of a socially disvalued group, or being in the situation of lacking important social goods can place patients at a distinct disadvantage.

[41] Educate Inspire Change. (2019, April 25). How many people of the world have a college degree? https://educateinspirechange.org/alternative-news/how-many-people-of-the-world-have-a-college-degree/
[42] Wikipedia. (2008, December 31). Education index. Wikipedia, the free encyclopedia. Retrieved February 2, 2021, from https://en.wikipedia.org/wiki/Education_Index

While there are different cultures and traditions of medicine around the world, differentiation between medical and lay audiences can be considered a homogenous global framework for understanding the ethical benefits and risks of help-seeking DTC. No culture has eliminated vulnerabilities in lay populations, and it is a fair assumption that physicians around the world are equally capable of interpreting all forms of DTC. The majority of the American lay public as well as a greater majority of the global public evaluate health information through the lens of trust in medicine, as opposed to enjoying true health science literacy.

Broad global consensus has been reached that DTC and advertising by industry to the medical community is acceptable. The medical community is trained with capacity to judge the value of pharmaceutical speech. In the lay population, while global basic literacy rates are strikingly high, a significant gap exists between basic literacy and health literacy. Compounded by Kipnis' framework of vulnerabilities in the lay population, PCPR DTC may create more harm than good. Adequate protections to protect lay audiences are essential if industry sponsored help-seeking DTC is to be made available globally.

7. Regulation: Authorize the WHO to Lead Enforceable International Regulation

To address lay vulnerabilities, regulation has offered protections. Any discussion of the legal/regulatory landscape governing DTC is complicated by the incredible patchwork of national, provincial, state, even city regulations around the world. In the United States, the Office of Prescription Drug Promotion (OPDP) within FDA is responsible for oversight. "Within OPDP, the FDA's Center for Drug Evaluation and Research (CDER) ensures that companies that sell prescription drugs also provide information that is truthful, balanced, and accurately described. CDER's Office of Prescription Drug Promotion (OPDP) oversees prescription drug ad activities. OPDP does this work by: (1) looking for and taking action against

advertisements that violate the law; (2) educating industry and others about the specifics of the law; and (3) encouraging better communication of promotional information provided both to healthcare professionals and to consumers."[43] "In the United States, the Federal Food, Drug, and Cosmetic Act (FDCA) and Title 21 of the Code of Federal Regulations Part 202 (21 CFR Part 202) primarily govern prescription drug advertising and promotion. Together, the FDCA and 21 CFR Part 202 regulate how pharmaceutical companies can promote prescription drugs to both health care professionals and consumers."[44] Concurrent regulatory bodies around the world are charged with similar missions. In Europe, the European Medicines Agency (EMA), "is responsible for the scientific evaluation, primarily of innovative and high-technology medicines developed by pharmaceutical companies for use in the EU. EMA was established in 1995 to ensure the best use of scientific resources across Europe for the evaluation, supervision and pharmacovigilance of medicines."[45]

DTC is regulated at the national level around the world with a clear majority of nations opting for more stringent regulation than the United States and New Zealand. In the United States, "no federal law has ever banned DTC advertising. Until the mid-1980s, drug companies gave information about prescription drugs only to doctors and pharmacists. When these professionals thought it appropriate, they gave that information to their patients. However, during the 1980s, some drug companies started to give the general public more direct access to

[43] Background on drug advertising. (2015, June 19). U.S. Food and Drug Administration. https://www.fda.gov/drugs/prescription-drug-advertising/background-drug-advertising.
[44] Marwah, U. (2018, February 26). Prescription drug advertising and promotion regulations and enforcement in select global markets. Food and Drug Law Institute (FDLI). https://www.fdli.org/2017/08/prescription-drug-advertising-promotion-regulations-enforcement-select-global-markets/
[45] European Medines Agency. (2016). European Medicines Agency. https://www.ema.europa.eu/en/documents/leaflet/european-regulatory-system-medicines-european-medicines-agency-consistent-approach-medicines_en.pdf

this information through DTC ads."[46] The regulatory architecture last evolved in the United States in 2011 with the formation of the Office of Prescription Drug Promotion (OPDP). According to FDA, with increased scope, the review of submissions by pharmaceutical companies is OPDP's priority. OPDP routinely evaluates claims by requesting evidence in support. "If not supported directly by the approved labeling… or… if evidence is not available or inadequate, a violation is cited… by OPDP."[47] Enforcement methodologies include attending professional conferences and exhibit halls, competitor complaints, health professional complaints, and others.

According to Britt Thompson, EVP, strategy and business transformation, Evoke Group, "given that the internet as we know it wasn't around when the original drug-ad regulations were written, the digital advertising rules have largely been codified via FDA guidances. The No. 1 rule applies across all media, but applying it to social media is obviously tricky. If the risk information occupies 45 seconds of a broadcast ad, it's nigh impossible to squeeze it into a tweet. The FDA released two guidance documents about drug promotion online and on social media in 2014, but they were not as comprehensive as expected."[48] FDA has issued four associated guidances including Internet/Social Media Platforms with Character Space Limitations Presenting Risk and Benefit Information for Prescription Drugs and Medical Devices, Internet/Social Media Platforms: Correcting Independent Third-Party Misinformation About Prescription Drugs and Medical Devices, Fulfilling Regulatory Requirements for Postmarketing

[46] U.S. Food and Drug Agency. (2015, June 19). Background on drug advertising. U.S. Food and Drug Administration. https://www.fda.gov/drugs/prescription-drug-advertising/background-drug-advertising#
[47] Pharmafield. (2005, December 1). Pharmaceutical direct-to-consumer advertising in Europe. https://pharmafield.co.uk/in_depth/pharmaceutical-direct-to-consumer-advertising-in-europe/
[48] Thompson, B. (2019, April 5). MM&M's annotated guide to the most essential DTC regulations and requirements - Regulatory - MM&M - Medical marketing and media. MM&M - Medical Marketing and Media. https://www.mmm-online.com/home/channel/regulatory/mmms-annotated-guide-to-the-most-essential-dtc-regulations-and-requirements/

Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics, and Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices.[49]

In the European Union, Article 88 of Directive 2001/83/EC sets the pharmaceutical marketing rules, prohibiting advertising of prescription-only medicines. The interpretation of Article 88 varies from country to country. "While advertising non-prescription medicines to the public is permitted in the UK (some limitations are provided in the Advertising Regulations to regulate the same), DTC advertising of prescription-only medicines is strictly prohibited as per the Advertising Regulations [of] 1994 (as amended), which implement EU Directive 92/28/EC."[50] Yet, like other countries, policy in the UK is less than binary. For example, informative, disease state questions may be answered in a DTC format provided no product claims are made in the UK.

"In Europe's largest drug market, Germany, the rules against DTCA of prescription pharma products are as stringent as those in other EU countries. In Germany, the Heilmittelwerbegesetz or HWG ('The Law on Advertising in the Field of Healthcare') governs pharma advertising. The regulations ban the promotion of product brands where the disease has only one treatment option available in the market. It has also become mandatory for advertisements to advise the public to consult a doctor or pharmacist. Expert opinions, product recommendations, healthcare professional advice and certain graphic representations are not permitted."[51]

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[49] Food And Drug Administration. (2020, September 4). For industry: Using social media. U.S. Food and Drug Administration. https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/industry-using-social-media

[50] Ibid.

[51] Ibid.

Other countries within the EU have adopted nuances to the general regulation. In the case of France, reimbursement is associated with the ethical equation such that only non-prescription products unreimbursed by the social security system, may be advertised. On the issue of disease state awareness, provided a product is not mentioned, advertising is permissible. In the Case of Spain, DTC is permitted only for non-critical medicines.

In India, "the business of medicines is regulated by the Drug and Cosmetics Act, 1940 (DCA) and the Drugs and Cosmetics Rules, 1945 (DCR). Until 2015, the DCA and DCR did not regulate DTC advertising except for the content that appeared on the label of the product."[52] Ladani notes the DCR currently stipulates that advertising in the 'public interest' is insufficient as a basis to advertise. Currently, the DCR includes several Schedules, X, H, and H1 which prohibit any and all advertising.

Outside the United States and the European Union, "pharmaceutical standards and regulatory systems across the world remain in many countries fragile, uneven and highly dependent on aid and technical support from international donors. The weakness of the regulatory apparatus in many pharmaceutical markets was recently illustrated in a study that looked at least developed countries. Olsson et al. (2010) found that less than half of least-developed countries publically funded their pharmaceutical regulatory agencies [19]. Moreover, many state institutions with the mandate to approve, review, and regulate pharmaceutical products in the survey were found to be highly dependent on financing from international organizations."[53]

[52] Direct-to-consumer advertising of medicines and medical devices — a call for action! (2018, August 14). Express Pharma. https://www.expresspharma.in/management-pharma/direct-to-consumer-advertising-of-medicines-and-medical-devices-a-call-for-action-2

[53] Pezzola, A. (2016, December 20). Global pharmaceutical regulation: The challenge of integration for developing states. PubMed Central (PMC). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5175325/

Any discussion of global DTC regulation revision must acknowledge the prevalence of disregard for existing DTC regulations and laws. In many parts of the world, the national regulatory frameworks managing DTC predate the digital revolution of the internet. Indian regulation dates to the 1955 Drugs and Magic Remedies (Objectionable Advertisements) Rules. Nigeria's Drug Products Advertisement Regulations, S.1 15 date to 1995. China's regulation "by two main statutes, the Advertisement Law ("AL"), promulgated in 1994, and the Drug Administration Law ("DAL"), promulgated in 2001"[54] are nearly twenty years old. Countries that have revisited regulation in roughly the last decade include Bangladesh, Brazil, Indonesia, and Russia.

Various national regulations acknowledge that educational opportunities exist with help-seeking DTC. As an example, in Bangladesh, "with the prior approval of [the] Drug Regulatory Authority, substantive, educational and public awareness type of advertisement on oral rehydration salt, family planning drugs and devices, water purifying drugs, antiseptic drugs and vaccines used in expanded program on immunization [are] permitted."[55] What is lacking is consensus through regulation on issues deemed in the public good in some countries, but not others. Along these lines, Brazilian regulation permits the state to advertise generics while prohibiting industry from the same. By way of comparison, if medicine can cooperate to publish international care guidelines, international pharma ought to be able to form a standardized global DTC consensus that improves health internationally. Simplified, streamlined global regulation that takes borderless internet communication into account is desperately needed. While FDA has

[54] Ma and Nan Lou, F. J. (2013, May). Regulation of Drug Promotion in China. Covington & Burling LLP | We help clients navigate issues at the intersection of law and policy around the world. https://www.cov.com/~/media/files/corporate/publications/2013/05/regulation_of_drug_promotion.pdf
[55] Directorate General of Drug Administration (Bangladesh). (2016). National Drug Policy (English version). www.dgda.gov. https://www.dgda.gov.bd/index.php/laws-and-policies/261-national-drug-policy-2016-english-version

issued multiple guidances related to new technologies, a globalized, universally respected approach that acknowledges the borderless context of the internet is greatly needed.

Buried in selling, general, and administrative expenses, legal expenses are exceedingly difficult to pinpoint in the financial disclosures of the global pharmaceutical companies. For the most part, reporting refers to ongoing litigation companies are party to, not the actual cost of representation. "Johnson & Johnson's litigation expenses have been on a rise over the past few years. They grew from $141 million in 2015 to around $2.0 billion in 2018. This represents an average growth rate of 197%."[56] A correlation between pending litigation and legal expenses is expected in the case of Johnson & Johnson, however base expenses suggest immense resources are being wasted from a value perspective. With a reduction in duplicate regulations, a reduction in legal expenses could be realized, and partial that expense reallocated to the direct benefit of patients.

Given the global nature of pharmaceutical companies, a compromise solution would be to grant the World Health Organization regulatory authority over all DTC communications, with simple regulation that permits help-seeking DTC, and maintains a ban on PCPR DTC. A checkpoint on relational 10% spend would be a necessary component. A counter argument could be made to approach the issue by enacting specific regulation in the most valuable national markets as a trickle-down approach. However, because of borderless internet communications, regulatory havens would undermine success.

[56] Trefis. (n.d.). How are rising litigation charges impacting Johnson & Johnson's earnings? Retrieved February 6, 2021, from https://dashboards.trefis.com/no-login-required/09qN3bDn/How-Are-Rising-Litigation-Charges-Impacting-Johnson-Johnson-s-Earnings-?from=forbes

8. Commercial Speech: Mandate Comprehensible Help-Seeking Speech

Commercial speech has been curtailed by national governments around the world, as well as the United States to provide protections against false and misleading claims. Under American law, corporations maintain the same rights as citizens, with expressive rights. Sentiments run against the notion of corporations' morally based expressive rights being on par with individuals. Further, "there have been calls in the U.S. for a moratorium on DTCA to curtail the negative effects of drug advertisements."[57] However, "such a proposal is likely to gain little traction since drug advertising falls under courts' expanding protection of 'commercial free speech' under the First Amendment."[58] "Tamara Piety, a professor at the University of Tulsa College of Law, has written prolifically on the subject in law review articles and in her *book Brandishing the First Amendment: Commercial Expression in America.* She argues that this expansion of the First Amendment could erode the ability for government to regulate commerce to the point where New Deal-era consumer and safety protections are undermined."[59]

While FDA regulations curtail pharmaceutical manufacturers from making promotional claims outside product labeling, legal precedent has thrown FDA regulation into question. In United States v. Caronia, the issue of off-label promotion was raised, and the court sided with industry. "Overturning the conviction of a sales representative who was found to have engaged in off-label promotion of a prescription drug, a three-judge panel of the U.S. Court of Appeals for the Second Circuit (New York) held in United States v. Caronia that the government cannot

[57] Stange KC. Time to ban direct-to-consumer prescription drug marketing. Ann Fam Med. 2007;5(2):101-104.
[58] Noah L. Truth or consequences?: Commercial free speech vs. public health promotion (at the FDA). Health Matrix Clevel. 2011;21(1):31-95.
[59] Zarrot, E. (2015, September 1). Commercial speech and the evolution of the First Amendment. Constitutional Accountability Center. https://www.theusconstitution.org/news/commercial-speech-and-the-evolution-of-the-first-amendment/

prosecute pharmaceutical manufacturers and their representatives under the [Food, Drug, and Cosmetic Act] for speech promoting the lawful, off-label use of an FDA-approved drug."[60]

In Sorrell v. IMS in 2011, regarding the Vermont Pharmaceutical Data Mining Law, the United States Supreme Court struck down a Vermont statue over First Amendment violations. "In application of First Amendment principles, the Court found the Vermont law to be discriminatory in that it suppressed a particularly effective, albeit distasteful, message."[61] The majority summarized, "if pharmaceutical marketing affects treatment decisions, it does so because doctors find it persuasive, and the fear that speech might persuade provides no lawful basis for quieting it."[62]

The 2015 Amarin Case further undermined FDA regulation with the "proposed settlement [being] the first time the FDA has conceded that pharmaceutical companies may engage in truthful and non-misleading speech promoting the off label use of the prescription drugs. While the settlement is promising, and certainly represents a significant final chapter in case that has dramatically impacted the FDA's enforcement landscape, it also reminds companies the possibility that the FDA and the Department of Justice (DOJ) will begin to pursue off-label cases based on false or misleading speech or conduct."[63] Following Amarin, Pacira pharmaceuticals obtained a similar judgement against FDA regarding commercial speech regarding Exparel.

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[60] *United States v. Caronia, No. 09-5006 (2d Cir. 2012)*. (n.d.). Justia Law. https://law.justia.com/cases/federal/appellate-courts/ca2/09-5006/09-5006-2012-12-03.html

[61] Boumil, M. (2013, January 9). Off-label marketing and the First Amendment | NEJM. New England Journal of Medicine. https://www.nejm.org/doi/full/10.1056/nejmp1214926

[62] Ibid.

[63] Palmer, E. (2016, March 9). With FDA settlement, tiny Amarin creates opening for Pharma in off-label marketing. FiercePharma. https://www.fiercepharma.com/pharma/fda-settlement-tiny-amarin-creates-opening-for-pharma-off-label-marketing

PCPR DTC, like all pharmaceutical marketing, is categorically advertising. Consequently, “commercial speech occupies a unique role as a free speech exception. While there is no complete exception, legal advocates recognize it as having diminished protection."[64] Misleading advertising may be restricted and false advertising can be penalized. “Commercial advertising may be restricted in ways that other speech can't if a substantial governmental interest is advanced, and that restriction supports that interest as well as not being overly broad.”[65] “This doctrine of limited protection for advertisements is due to a balancing inherent in the policy explanations for the rule, namely that other types of speech (for example, political) are much more important.”[66]

Globally, “freedom of speech is granted unambiguous protection in international law by the International Covenant on Civil and Political Rights which is binding [in] around 150 nations.”[67] Pharmaceutical speech has been treated internationally as advertising, much in the same manner as the American perspective.

Piety’s concerns of radical first amendment expansion seems an unlikely future - commercial speech is unspecific to the pharmaceutical industry and applies across sectors with broad reaching implications. Historically, before increased regulatory enforcement in the 2000s, and the PhRMA guidelines, direct to physician pharmaceutical marketing was rife with misleading and unrepresentative claims. Non-peer reviewed articles and journals were

[64] Ruane, K. A. (2014, September 8). Freedom of Speech and Press: Exceptions to the First Amendment. Federation of American Scientists. https://fas.org/sgp/crs/misc/95-815.pdf
[65] Wikipedia. (2020, December 31). Central Hudson gas & electric Corp. v. Public Service Commission. Wikipedia, the free encyclopedia. Retrieved January 19, 2021, from https://en.wikipedia.org/wiki/Central_Hudson_Gas_%26_Electric_Corp._v._Public_Service_Commission
[66] Ruane, K. A. (2014, September 8). Freedom of Speech and Press: Exceptions to the First Amendment. Federation of American Scientists. https://fas.org/sgp/crs/misc/95-815.pdf
[67] Wikipedia. (2002, January 16). Freedom of speech by country. Wikipedia, the free encyclopedia. Retrieved January 19, 2021, from https://en.wikipedia.org/wiki/Freedom_of_speech_by_country

frequently promulgated by industry and claims were routinely made outside of product labeling. With other commercial sectors leading the way, any expansion of free speech to broaden commercial speech would surely incur the same practices again by pharma.

Maintaining the present balance in the United States represents a fair tradeoff between consumer protection and the voices of industry. The American interpretation of the limits of commercial speech should be adopted on a global level. The permission of help-seeking DTC in countries lacking enforcement of local law will trigger competition between regulated and non-regulated sources of health information. According to Diaz and colleagues, research suggests lay audiences have long been scrutinizing the quality of medical information they find online. "When [US] patients were asked to identify factors associated with a reliable Internet health site, sponsorship by a medical society was chosen by seventy-two percent of respondents (197 of 274). Other important factors included site recommended by a physician or health care professional, 60% (165 of 274), sponsored by a university, 59% (162 of 274), and sponsored by a hospital/HMO, 51% (140 of 274). Less-frequently selected factors were sponsored by a nonprofit organization, 30% (81 of 274), site recommended on TV, radio, newspaper, or magazine, 18% (49 of 274), sponsored by a pharmaceutical company, 16% (44 of 274) and "site advertised on TV, radio, newspaper, magazine, or Internet. 13% (35 of 274)"[68]

While DTC exists within commercial speech in the United States, Frosch cautions that "analyses of the content of ads find that most DTCA lacks information important to help consumers decide about the benefits and risks of prescription drugs. Benefits of drugs are often described in vague terms or through narratives that exaggerate the magnitude of benefits. In print

[68] Diaz, J. A. (2002). Patients' use of the internet for medical information. PubMed Central (PMC). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1495021/

[and therefore internet] ads, most of the content exceeds the eighth-grade reading level recommended for the general public."[69] Help-seeking DTC ought to remain within the realm of commercial speech in order to retain restrictions. Given global commercial speech frameworks often align with the American perspective, provisions to address lay vulnerabilities could be made in a global context to limit language to 6th grade levels in the regional language.

9. Addressing Bias

Health information is inherently biased regardless of sponsorship origin, be that government, academic, or industry. If an ethical argument is to be made for the superiority of non-pharmaceutical industry sponsorship of independent education, the publisher WebMD could serve as a contrasting case example. According to WebMD, they "provide credible information, supportive communities, and in-depth reference material about health subjects that matter to you. We are a source for original and timely health information as well as material from well-known content providers."[70] WebMD carries certifications from HONcode and Healthguard.[71] According to HONcode, certified sites meet their criteria for authority, complementarity, privacy, attribution, justifiability, transparency, financial disclosure, and advertising policy. Whether HONcode ethical certification truly addresses lay vulnerabilities remains an open question.

Yet, the WebMD experience culminates in referrals, based on commissions, to health systems. WebMD's business model contains ethical flaws on the order of pharmaceutical sales

[69] Frosch, D. L. (2010, March). Direct-To-Consumer Advertising of Prescription Drugs. Welcome to LDI | LDI. https://ldi.upenn.edu/sites/default/files/pdf/IssueBrief%2015_3.pdf
[70] WebMD. (2017, February 16). *What we do for our users*. https://www.webmd.com/about-webmd-policies/about-what-we-do-for-our-users
[71] WebMD. (n.d.). About WebMD. https://www.webmd.com/about-webmd-policies/default.htm

and reminder advertisements. Healthguard's corporate sponsorship from Mount Sinai and Publicis Health Media are direct conflicts of interest.

Independent third party implementation of help-seeking DTC can insure communications do not wade into sales or reminder categorized advertising. With increased financial transparency, and an ethical separation, the American rules surrounding sponsorship of Continuing Medical Education (CME) for physicians by industry could serve as a successful global model to decouple industry's for-profit motivations from help-seeking advertising. Mitigating off-label promotion liabilities, third party implementation garners tertiary benefits to industry as well. Article 2 of the elements of the Association of Medical Media's Code of Ethics could become a backbone for pharmaceutical industry sponsored help-seeking DTC. Article 2 – " No editorial material will be published in return for advertising consideration, and no editorial material will be published in exchange for monetary compensation except as provided for editorial supplements by the International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals and the World Association of Medical Editors (WAME) Recommendations on Publication Ethics Policies for Medical Journals."[72]

10. Technology Solutions – Protecting Populations and Increased Consumer Protections

Emerging technologies have the potential to improve health in otherwise underserved populations. While DTC advertising may have resided on traditional media such as radio, television, and print when popularized in the 1980s and 1990s, internet based advertising and media have surpassed in terms of influence. In 2018, eMarketer editors noted, "this year, mobile

[72] Deak, T. V. (n.d.). Amm. AMM. https://www.ammonline.org/code-of-ethics

will surpass TV ad spending by more than $6 billion, according to our latest ad spending forecast. By 2020, the channel will represent 43% of total media ad spending in the US—a greater percentage than all traditional media combined."[73] The promise of burgeoning internet technologies is boundless, and increasingly blind to national boundaries. "Digital content is at the heart of the emergence of a cultural renaissance thanks to the opportunity for niche content creators to distribute their products on the unlimited shelf space of the Internet. Broadcasters, publishers, and other traditional media distributors that were constrained by limited space for their content offline have seen their business models disrupted."[74]

Taking advantage of emerging technologies, help-seeking DTC approaches may ethically identify sub-populations who otherwise may not have had access to care on unprecedented scales. With internet based commercial targeting algorithms, the opportunity to focus-target and power of help-seeking DTC has never been greater. "There's another vast new frontier to watch for regulatory battles over compliance, too. As digital and social media increase in ubiquity, DTC pharmaceutical ads have proliferated on these platforms and research has shifted its focus to match, producing scholarly content analyses of digital ads, social media content and warning letters issued by the FDA over online ads. A study published in 2015 in BMC Health Services Research found that internet-based direct-to-consumer advertising increased 109 percent between 2005 [and] 2009, while most other media experienced declines in ad expenditures."[75]

[73] EMarketer Editors. (2018, October 16). Mobile ad spending to surpass all traditional media combined by 2020. Insider Intelligence. https://www.emarketer.com/content/mobile-ad-spending-to-surpass-all-traditional-media-combined-by-2020
[74] PricewaterhouseCoopers. (2017, January 4). Content democratization: How the internet is fueling the growth of creative economies. PwC. https://www.strategyand.pwc.com/gx/en/insights/2017/content-democratization.html
[75] Reichel, C. (2018, May 2). Direct-to-consumer drug advertising spikes demand. Journalist's Resource. https://journalistsresource.org/studies/government/health-care/direct-to-consumer-prescription-drugs/

Technology in medicine has evolved at a staggering rate over the last 50 years. With mobile technologies at the center of many innovations, serious issues around privacy, what constitutes protected health information, and disclosure are at the heart of many ethical debates. A security and privacy gap is growing between general data and health data. Outside US Health Insurance Portability and Accountability Act (HIPAA) laws, Apple's 'iwatch' can assess the wearer for atrial fibrillation, while other wearable devices track activity, heart rate, body temperature, and a myriad of other metrics. The United States and a host of other countries provide little or no protection to technologies such as these.

While internet based marketing is on the rise, perceptions around internet based health campaigns are perceived differently than those in traditional campaigns. "Menon, Deshpande, Perri, and Zinkhan (2002) [examined] in Health Marketing Quarterly … how key demographic, predispositional, and media factors are associated with consumer trust in on-line prescription drug information and the impact of trust in on-line drug information on ad-promoted behavior following exposure to direct-to-consumer (DTC) advertising. Four major findings are reported: (1) on-line drug information is not highly trusted; (2) trust in on-line drug information is not differentially affected by consumer demographic or predispositional characteristics; (3) trust in the traditional media of DTC advertising is predictive of trust in on-line drug information; and (4) trust in on-line drug information is associated directly with specific types of ad-promoted behavior following exposure to DTC advertising."[76]

Employing stifling user agreements that most end-users are unable to comprehend, privately held internet search providers dominate the flow of information on the internet. Non-

[76] Huh, J. (2007, February 23). Factors affecting trust in on-line prescription drug information and impact of trust on behavior following exposure to DTC advertising. Taylor & Francis. https://www.tandfonline.com/doi/abs/10.1080/10810730500326716

anonymized searches that yield DTC websites are being leveraged in unforeseen ways. Artificial intelligence companies are building data pictures based on DTC interactions of users in startling ways that amount to unethical breaches of medical privacy. Like credit scores, data of consumers of DTC is for sale to insurers for the purpose of screening populations and removing high risk individuals from pools. Current protections for consumers interacting with internet based DTC are inadequate at best, to completely non-existent.

With "the global number of smartphone users … reach[ing] three billion by 2018", [77] never before has there been a time of greater access to help-seeking related content. However, 2019 data from Newzoo suggests smartphone penetration remains below 11% in 145 countries. If concepts such as DTC for help-seeking based health improvement or telemedicine are to succeed, much work is yet to be done. The United States at 79% penetration[78] in 2019 is less than representative of the global situation.

With 47% of people in the developing world reporting internet access in 2019, [79] the current opportunity to improve global health via help-seeking DTC is tangible. Technological solutions for expanding help-seeking DTC to global communities are inevitable, but timelines exceed acceptability. Short term, pharmaceutical manufacturers and marketers have an obligation to respect local law, limiting content regionally via internet technology. More than a simple acknowledgement of being a US based prescriber or patient, pharmaceutical companies limiting content by browsing locale respects regional autonomy. First steps towards a global

[77] Kooista, J. (2018). Mobile market trends App market revenues & forecasts Mobile brand & model usage Smartphone penetration. https://resources.newzoo.com. https://resources.newzoo.com/hubfs/Reports/Newzoo_2018_Global_Mobile_Market_Report_Free.pdf
[78] Ibid.
[79] International Telecomunicaion Union. (2021). Measuring digital development: Facts and figures 2019. https://www.itu.int/en/ITU-D/Statistics/Pages/facts/default.aspx

solution include the cessation of pharmaceutical companies allowing marketing content into regulated nations that prohibit sales and sales reminder advertisements.

Technology must be part of a global help-seeking DTC approach incorporating mechanisms to collaborate with regulators. According to Knoppers, "a brief comparative overview of international and national developments on the confidentiality of health information over the last half century must cover (1) the right of privacy, (2) medical confidentiality per se, and (3) the protection of personal data. Together they overlap and sometimes commingle."[80] "Over 80 countries and independent territories, including nearly every country in Europe and many in Latin America and the Caribbean, Asia, and Africa, have now adopted comprehensive data protection laws.[1] The European Union has the General Data Protection Regulation (GDPR),[2] in force since May 25, 2018. The United States is notable for not having adopted a comprehensive information privacy law, but rather having adopted limited sectoral laws in some areas like the California Consumer Privacy Act (CCPA).[3]"[81] As the General Data Protection Regulation (GDPR) gains prominence, the "literature regarding mHealth applications over the past several years demonstrates that the security of data storage and transmission remains a concern, and the question of data "ownership" is complicated by the multiple stakeholders who have access to such data in the current ecosystem, often without the knowledge of the subject of the data. Consumers are often uneducated regarding the ways a service may collect and transmit their data to third parties; yet even when they are aware of the implication of vendor terms of

[80] Knoppers, B. M. (2000). Confidentiality of health information: International comparative approaches - Protecting data privacy in health services research - NCBI bookshelf. National Center for Biotechnology Information. https://www.ncbi.nlm.nih.gov/books/NBK222816/

[81] Information privacy law. (2005, October 26). Wikipedia, the free encyclopedia. Retrieved February 12, 2021, from https://en.wikipedia.org/wiki/Information_privacy_law

service, most users do not read these policies before consenting due to policy length and complexity."[82]

While general data protection laws are improving, international health data protection law could be a framework to open countries to the potential of help-seeking DTC. Ensuring special protections for anonymity and preventing tracking would be essential elements. Incorporation of American HIPAA standards would be supportive. With the reasonable success of the GDRP, the European Union makes a good candidate for the introduction of health data protections.

11. Conclusions

As expressed through industry mission statements, the pharmaceutical industry has a moral mandate to improve health. Health systems around the world, especially in developing countries, lack the resources to fund health education. Through education, we can address fundamental rights to care, reduce lay vulnerabilities, increase capacity for making informed health decisions, and ethically aid populations around the world. Help-seeking DTC, meaning dedicated health education websites, videos, and unbranded content has the promise to improve health around the world. The pathway to realizing a benefit includes support from industry, awareness of audiences and accounting for their vulnerabilities, reducing regulation and empowering the WHO to ensure simplified rules are enforced, mandating comprehensible speech on the level of those most in need, engineering bias out of the equation, and taking advantage of emerging technologies while ensuring privacy is maintained. Help-seeking DTC has the capability to expand global health literacy. Help-seeking DTC approaches may further ethically identify sub-populations who otherwise may not have had access to care. The availability of substantiated

[82] Galvin, H. (2020, August). Developments in privacy and data ownership in mobile health technologies, 2016-2019. PubMed Central (PMC). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7442507/

medical education from genuine authorities has the ability to offset the negative impacts of baseless claims, elevating the threshold of medical credibility.

The pharmaceutical industry must reallocate resources to fulfill an ethical responsibility to support basic global health education. Recognizing pharmaceutical business is a cyclical endeavor, partial reallocation of sales and marketing expenses away from product claims and reminders towards help-seeking DTC is possible without disruption of business cycles. A 10% budgetary spend mandate for help-seeking DTC relative to global sales and marketing expenses of branded medications could be an effective rule to finance independent health education, and improve global health equity. While other solutions such as government programs and educational systems exist to improve global health, help-seeking DTC is positioned to make a greater impact in less time. Ministries of health in third world countries lack basic resources as evidenced by generalized education levels and modes of financing. Counter to approaches that entail incurment of international government loans or other debt structures, industry sponsored help-seeking DTC comes at a practical discount.

Delineation between medical and lay populations is essential. Tremendous global education gaps exist that help-seeking DTC could address. Acknowledging lay audience vulnerabilities by mandating limitations on communication complexity will increase effectiveness. Thus, restrictions on education should include a mandate of language not to exceed a sixth grade reading level.

Robust regulation in the United States and around the world has, to a great degree, controlled pharmaceutical speech. Granting the World Health Organization regulatory authority to permit help-seeking DTC and maintain bans on PCPR DTC is a fair compromise that benefits patients. Ultimately, with reductions in duplicate regulations surrounding help-

seeking DTC, the pharmaceutical industry could reduce legal representation expenses and redirect resources to ethical missions of beneficence to patients

While freedom of speech may be at the core of proponents' arguments, the legal categorization of pharmaceutical speech as commercial has ensured protections from misleading and untrue claims. Existing commercial speech laws represent a global framework that help-seeking DTC could exist within. Allowing help-seeking DTC to be considered under the broader categorization of free speech would be a regression.

Reduction of bias and increased independence of help-seeking DTC can be achieved through decoupling sponsors from content as has been realized in the sponsorship of American CME to physicians. The internet and technology are rapidly changing the environment in which DTC exists. Because the European GDRP has gained acceptance in so many parts of the world, it could serve as a reference point for new health specific help-seeking DTC international law in concert with oversight by WHO. American conceptions of health information privacy, the Health Insurance Portability and Accountability Act, could be integrated.

The current landscape is one of significant legal and regulatory constraint in most parts of the world for any type of DTC, and an expanding market in the United States amongst all three FDA defined categories of DTC. From a philosophical perspective, industry and medicine have more in common attitudinally than might be expected from the onset. Fundamental is compromise, industry adherence to regulation and law, and always keeping the patient first in mind.